

REMARKS

Claims 1-14 and 17 are pending. Applicants have cancelled claim 12 without prejudice and added new claim 18. Claims 1-11, 13, 14, 17, and 18 will therefore be pending upon entry of the proposed amendments.

Claim 1 as presently amended is now directed to “[a] **purified** compound of general formula I.” Support for this amendment can be found throughout the specification, e.g., at the paragraph bridging pages 3 and 4; the third paragraph following the table at page 20; and Example 2 (see pages 22-25).

Support for the amendments to claim 10 can be found throughout the specification, e.g., at the paragraph bridging pages 3 and 4; the two paragraphs that follow the chemical structure at page 12; and Examples 1 and 2 (see pages 22-25). Applicants have amended claim 11 to be consistent with the language recited in claim 10 as presently amended. Applicants have amended claim 13 to depend from claim 10 instead of claim 12 (now cancelled).

The subject to be deleted from claims 3, 4, 14, and 17 has been now indicated with a strikethrough only (i.e., the double brackets have been removed).

Support for new claim 18 can be found throughout the specification, e.g., at the paragraph bridging pages 3 and 4.

No new matter is introduced by these amendments.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 10-13 are rejected for allegedly failing to comply with the written description requirement of under 35 U.S.C. § 112, first paragraph. According to the Office:

It is apparent that the cell line ES7-008 is required to practice the claimed invention. Note that cell line ES7-008 is recited in claim 13, and is the only specifically disclosed cell line capable of producing the intended compounds. As a required element, cell line ES7-008 must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirement of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of cell line ES7-008. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining cell line ES7-008, and cell line ES7-008 does not appear to be a readily available material. Deposit of cell line ES7-008 would satisfy the enablement requirements of 35 U.S.C. 112, first paragraph.

The rejection of claim 12 is moot in view of its cancellation. The rejection has been met, in part, by amending the claims.

1. Deposit of strain ES7-008

As acknowledged in the present Office Action, a deposit of strain ES7-008 has been made under the terms of the Budapest Treaty. See specification at page 12, first paragraph:

Compound IB-01211 is preferably obtained from an actinomycete, named strain ES7-008. A culture of this strain has been deposited in the Colección Española de Cultivos Tipo at the University of Valencia, in Spain, under the accession number CECT 3358. This deposit has been made under the provisions of the Budapest Treaty.

Applicants provide herewith a copy of the deposit receipt and the viability statement, both of which are in Spanish. Applicants therefore have also provided an English language translation of both the deposit receipt and the viability statement along with a verification of the translation.

2. Claim 10 as presently amended is now drawn to (emphasis added):

A process for preparing a compound as defined in claim 1 which comprises (i) cultivating **a microorganism strain of the *Thermoactinomyces* genus capable of producing it** and (ii) isolating said compound from the cultured broth.

The taxonomic analysis of the strain ES7-008 shows that this strain is phylogenetically close to *Thermoactinomyces* genus (see specification at page 12, first paragraph; page 17, second full paragraph; and page 18, second full paragraph (bolded, underline emphasis added):

The microorganism strain ES7-008 is phylogenetically close to *Thermoactinomyces* genus. The organism was isolated from an unidentified marine sponge. The taxonomic methods were as follows. ...

Partial sequence of 16S rDNA was performed following standard procedures. The DNA of the organism was extracted after homogenization under liquid nitrogen. The 16S rDNA gene was amplified by the polymerase chain reaction using the eubacterial primers 27f and 1492r. The partial sequences were obtained using the primers 357r, 926r, and 1492r. All the primers used in this work were described by Lane, D.J. *Nucleic acid techniques in bacterial systematics*:115, 1991. ...

This sequence was confronted with the Gene Bank depository using the Blastn algorithm. The phylogenetic studies were performed using the Phylip package developed by Felsenstein, J. *Cladistics* 5:164, 1989. **A consensus phylogenetic tree was constructed after bootstrapping the sample. Strain ES7-008 was grouped with the *Thermoactinomyces* group.** A differentiating trait of strain ES7-008 with *Thermoactinomyces* is a lack of aerial mycelium and the need of salt for growth.

Applicants also provide "Appendix I" for the Examiner's consideration, which shows the differences between the *Thermoactinomyces* spp. ES7-008 and the *Streptomyces nobilis* JCM4274 strains. The latter is a different strain of a different genus, *Streptomyces nobilis* (see background section of specification), which is known to produce different compounds.

In addition, Applicants provide Kanoh, et al., *J.Antibiot.* **2005**, 58(4), 289-292. This reference describes that Mechercharmycin A, a compound that is identical to compound IB01211

of the specification (see, in particular, footnote 2 in Kanoh), can be produced by a *Thermoactinomyces sp.* bacteria. In view of the foregoing, Applicant submit that a person skilled in the art would therefore reasonably conclude that the claimed compounds could be produced by other microorganism strains of the *Thermoactinomyces* genus, in addition to the ES7-008 strain.

Applicants therefore respectfully request that the rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 101

Claims 1-8 and 10-12 are rejected because “the claimed invention is directed to non-statutory subject matter.

The rejection has been met by amending the claims. Claim 1 as presently amended is now directed to “[a] **purified** compound of general formula I.” Claim 10 now recites “**isolating** said compound from the cultured broth.” 35 U.S.C. 101 is satisfied when the “hand of man” has intervened in some way no matter how small. See, e.g., *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (Supreme Court, 1980). As such, Applicants respectfully request that the rejection be reconsidered and withdrawn in view of the foregoing amendments.

Applicant : Francisco Romero et al.
Serial No. : 10/562,079
Filed : December 22, 2005
Page : 12 of 12

Attorney's Docket No.: 14700-008US1 / F/USP288234

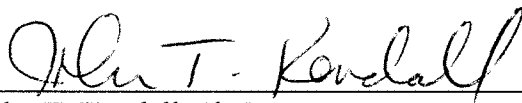
CONCLUSION

Applicants submit that all claims are in condition for allowance.

The fee in the amount of \$120 for the One Month Petition for Extension of Time fee ois being paid concurrently herewith on the Electronic Filing System (EFS) by way of a Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 14700-008US1F/USP288234.

Respectfully submitted,

Date: December 7, 2007



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Appendix 1

Both strains are taxonomically very different specially regarding their ribosomal sequences, metabolic requirements, salinity conditions, G+C content, or their fatty acid composition of membrane:

	13:0	i14:0	14:0	i15:0	A15:0	15:0	i16:1	i16:0	16:1	16:0	i17:1	i17:0	A17:0	17:1	17:0
Th	<1	<1	<1	<1	64.2	6.29	1.36	<1	4.52	<1	<1	14.68	4.14	1.45	<1
Sa	<1	6.52	<1	9.88	22.92	<1	5.50	25.29	<1	3.75	1.28	3.38	8.60	<1	<1

The following table classifies the phylogenetic differences:

	<i>Thermoactinomyces</i> spp. ES7-008	<i>Streptomyces nobilis</i> JCM4274
DOMAIN	<i>Bacteria</i>	<i>Bacteria</i>
PHYLUM	<i>Firmicutes</i>	<i>Actinobacteria</i>
CLASS	<i>Bacilli</i>	<i>Actinobacteria</i>
ORDER	<i>Bacillales</i>	<i>Actinomycetales</i>
FAMILY	<i>Thermoactinomycetaceae</i>	<i>Streptomycetaceae</i>
GENUS	<i>Thermoactinomyces</i>	<i>Streptomyces</i>
SPECIES	<i>Sp.</i>	<i>nobilis</i>
SUBSPECIES	<i>ES7-008</i>	<i>JCM 4274</i>

TRATADO DE BUDAPEST SOBRE EL RECONOCIMIENTO INTERNACIONAL
DEL DEPÓSITO DE MICROORGANISMOS A LOS FINES DEL
PROCEDIMIENTO EN MATERIA DE PATENTES

FORMULARIO INTERNACIONAL

DESTINATARIO Agustín Pérez-Arganda Ortega Instituto Biomar, S.A. Pol. Ind. de León. Edificio CEEI 24231 Onzonilla. León.		DECLARACIÓN DE VIABILIDAD, expedida en virtud de la Regla 10.2 por la AUTORIDAD INTERNACIONAL DE DEPÓSITO identificada en la parte inferior de esta página
NOMBRE Y DIRECCIÓN DE LA PARTE A LA QUE SE EXPIDE LA DECLARACIÓN SOBRE LA VIABILIDAD		
I. DEPOSITANTE		II. IDENTIFICACIÓN DEL MICROORGANISMO
Nombre: Agustín Pérez-Arganda Ortega Dirección: Instituto Biomar, S.A. Pol. Ind. de León. Edificio CEEI 24231 Onzonilla. León.		Número de orden atribuido por la AUTORIDAD INTERNACIONAL DE DEPÓSITO: CECT 3358 Fecha del depósito o de la transferencia ¹ : 21 de Febrero de 2002
III. DECLARACIÓN DE VIABILIDAD		
La viabilidad del microorganismo identificado en II ha sido controlada el 8 de Marzo de 2002 ² . En esa fecha el microorganismo <input checked="" type="checkbox"/> ³ era viable <input type="checkbox"/> ³ ya no era viable		

¹ Indíquese la fecha del depósito inicial o, si se ha efectuado un nuevo depósito o una transferencia, la más reciente de las fechas pertinentes (fecha del nuevo depósito o fecha de la transferencia).

² En los casos previstos en la Regla 10.2.a)ii) y iii), menciónese el control de viabilidad más reciente.

³ Márquese el recuadro correspondiente.

IV. CONDICIONES EN LAS QUE SE HA EFECTUADO EL CONTROL DE LA VIABILIDAD⁴

Crecimiento en los medios de cultivo adecuados a las temperaturas indicadas.

V. AUTORIDAD INTERNACIONAL DE DEPÓSITO

Nombre:
COLECCIÓN ESPAÑOLA DE CULTIVOS TIPO
(CECT).

Dirección:

Universidad de Valencia.

Edificio de Investigación.

Campus de Burjassot.

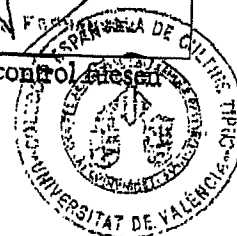
46100 Burjassot (Valencia) ESPAÑA

Firma(s) de la(s) persona(s)
competente(s) para representar a la
autoridad internacional de depósito
o del (de los) empleado(s) autorizado(s)

Fecha: 11 de marzo de 2002

FEDERICO DE TENDILLO FEDERICO DE TENDILLO

⁴ Deberá cumplimentarse si se ha solicitado esta información y si los resultados del control ~~arcsen~~ ^{arcsen} son negativos.



**BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
MICROORGANISMS DEPOSIT FOR PROCEDURE IN MATTER OF PATENTS**

INTERNATIONAL APPLICATION FORM

CONSIGNEE: Agustín Pérez-Arganda Ortega Instituto Biomar, S.A. Pol. Ind. de Leon. Edificio CEEI. 24231 Onzonilla (Leon)		DECLARATION OF VIABILITY. Issued by the INTERNATIONAL AUTHORITY OF DEPOSIT identified in the following page by reason of the Rule 10.2
NAME AND ADDRESS OF THE PART ISSUED THE DECLARATION OF VIABILITY		
I. DEPOSITARY		II. IDENTIFICATION OF THE MICROORGANISM
Name: Agustín Pérez-Arganda Ortega Address: Instituto Biomar, S.A. Pol. Ind. de León. Edificio CEEI 24231 Onzonilla. León		Number of order attributed by the INTERNATIONAL AUTHORITY OF DEPOSIT: CECT 3358 Date of the deposit or transfer ¹ : <u>February 21st 2002</u>
III. DECLARATION OF VIABILITY		
Viability of the microorganism identified in II has been controlled on March 8 th 2002 ² . On that date, the microorganism		
<div style="display: flex; justify-content: space-between; width: 100%;"> <div> <input checked="checked" type="checkbox"/> ³ Was viable </div> <div> <input type="checkbox"/> ³ Was not viable anymore </div> </div>		

¹ Please, indicate the date of the initial deposit, or if a new deposit or a transfer has been made, the most recent of the appropriate dates (date of the new deposit or date of the transfer).

² In the instances provided in the Rule 10.2 a)ii) and iii), please mention the most recent control of viability.

³ Tick the appropriate box.

IV. CONDITIONS IN WHICH THE VIABILITY ⁴ CONTROL HAS BEEN CARRIED OUT	
Growth in appropriate culture media at indicated temperatures	
V. INTERNATIONAL DEPOSIT AUTHORITY	
Name: Coleccion Española de Cultivos Tipo (CECT) Address: Universidad de Valencia, Edificio de Investigación. Campus de Burjassot 46100 Burjassot (Valencia) España (Note of the translator: Please, refer to the original stamp in the Spanish version)	Signatures of the person/people competent to represent the INTERNATIONAL AUTHORITY OF DEPOSIT or the authorized employee. Date: March 11 th 2002 (Note of the translator: Please, refer to the original signature and stamp in the Spanish version)

⁴ It should be filled in if this information has been requested and if the control results would be negative.

VERIFICATION OF TRANSLATION

I, (name and address of translator) Juan José González Blázquez
C/ FERNANDO OSSORIO N° 3 1° IZQ
28039 MADRID, SPAIN

am the translator of Deposit Receipt No. CECT3358 and I state that the following is a true translation to the best of my knowledge and belief.

(Signature of Translator)

(Dated)

J. José González
3 August 2006